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### General information about the entry

Entry name	CCR4_HUMAN
Primary accession number	P30991
Secondary accession numbers	O60835 P56438 Q9UKN2
Entered in Swiss-Prot in	Release 26, July 1993
Sequence was last modified in	Release 26, July 1993
Annotations were last modified in	Release 41, February 2003

### Name and origin of the protein

Protein name	C-X-C chemokine receptor type 4
Synonyms	CXC-R4 CXCR-4 Stromal cell-derived factor 1 receptor SDF-1 receptor Fusin Leukocyte-derived seven transmembrane domain receptor LESTR LCR1 FB22 NPYRL HM89 CD184 antigen
Gene name	CXCR4

From	<a href="#">Homo sapiens (Human)</a> [TaxID: 9606] <a href="#">Pan troglodytes (Chimpanzee)</a> [TaxID: 9598]
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Taxonomy	<a href="#">Eukaryota</a> ; <a href="#">Metazoa</a> ; <a href="#">Chordata</a> ; <a href="#">Craniata</a> ; <a href="#">Vertebrata</a> ; <a href="#">Euteleostomi</a> ; <a href="#">Mammalia</a> ; <a href="#">Eutheria</a> ; <a href="#">Primates</a> ; <a href="#">Catarrhini</a> ; <a href="#">Hominidae</a> ; <a href="#">Homo</a> .
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### References

- [1] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).  
SPECIES=Human;  
TISSUE=Lung;  
MEDLINE=93319629; PubMed=8329116; [NCBI, ExPASy, EBI, Israel, Japan]  
[Herzog H.](#), [Hort Y.J.](#), [Shine J.](#), [Selbie L.A.](#);  
"Molecular cloning, characterization, and localization of the human homolog to the reported bovine NPY Y3 receptor: lack of NPY binding and activation.";  
DNA Cell Biol. 12:465-471(1993).
- [2] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).  
SPECIES=Human;  
TISSUE=Fetal brain;  
MEDLINE=94052833; PubMed=8234909; [NCBI, ExPASy, EBI, Israel, Japan]  
[Jazin E.E.](#), [Yoo H.](#), [Blomqvist A.G.](#), [Yee F.](#), [Weng G.](#), [Walker M.W.](#), [Salon J.](#), [Larhammar D.](#), [Wahlestedt C.R.](#);  
"A proposed bovine neuropeptide Y (NPY) receptor cDNA clone, or its human homologue, confers neither NPY binding sites nor NPY responsiveness on transfected cells.";

Regul. Pept. 47:247-258(1993).

[3] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

**TISSUE**=Fetal spleen;

MEDLINE=93315164; PubMed=8325644; [NCBI, ExPASy, EBI, Israel, Japan]

Federspiel B., Melhado I.G., Duncan A.M., Delaney A.D., Schappert K.T., Clark-Lewis I., Jirik F.R.;

"Molecular cloning of the cDNA and chromosomal localization of the gene for a putative seven-transmembrane segment (7-TMS) receptor isolated from human spleen.";

Genomics 16:707-712(1993).

[4] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

**TISSUE**=Monocytes;

MEDLINE=94103215; PubMed=8276799; [NCBI, ExPASy, EBI, Israel, Japan]

Loetscher M., Geiser T., O'Reilly T., Zwahlen R., Baggiolini M., Moser B.;

"Cloning of a human seven-transmembrane domain receptor, LESTR, that is highly expressed in leukocytes.";

J. Biol. Chem. 269:232-237(1994).

[5] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

**TISSUE**=Monocytes;

MEDLINE=94092629; PubMed=7505609; [NCBI, ExPASy, EBI, Israel, Japan]

Nomura H., Nielsen B.W., Matsushima K.;

"Molecular cloning of cDNAs encoding a LD78 receptor and putative leukocyte chemotactic peptide receptors.";

Int. Immunol. 5:1239-1249(1993).

[6] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1), AND CHARACTERIZATION OF ITS HIV-1 CORECEPTOR FUNCTION.

MEDLINE=96217947; PubMed=8629022; [NCBI, ExPASy, EBI, Israel, Japan]

Feng Y., Broder C.C., Kennedy P.E., Berger E.A.;

"HIV-1 entry cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor.";

Science 272:872-877(1996).

[7] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

**TISSUE**=Peripheral blood leukocytes;

MEDLINE=98136183; PubMed=9468539; [NCBI, ExPASy, EBI, Israel, Japan]

Wegner S.A., Ehrenberg P.K., Chang G., Dayhoff D.E., Sleeker A.L., Michael N.L.;

"Genomic organization and functional characterization of the chemokine receptor CXCR4, a major entry co-receptor for human immunodeficiency virus type 1.";

J. Biol. Chem. 273:4754-4760(1998).

[8] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

MEDLINE=98258970; PubMed=9599023; [NCBI, ExPASy, EBI, Israel, Japan]

Caruz A., Samsom M., Alonso J.M., Alcami J., Baleux F., Virelizier J.L., Parmentier M., Arenzana-Seisdedos F.;

"Genomic organization and promoter characterization of human CXCR4 gene.";

FEBS Lett. 426:271-278(1998).

[9] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

MEDLINE=99408510; PubMed=10480633; [NCBI, ExPASy, EBI, Israel, Japan]

Xiao L., Weiss S.H., Qari S.H., Rudolph D., Zhao C., Denny T.N., Hodge T., Lal R.B.;

"Partial resistance to infection by R5X4 primary HIV type 1 isolates in an exposed-uninfected individual homozygous for CCR5 32-base pair deletion.";

AIDS Res. Hum. Retroviruses 15:1201-1208(1999).

[10] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

**SPECIES**=Human;

**TISSUE**=Peripheral blood lymphocytes;

MEDLINE=99095114; PubMed=9879064; [NCBI, ExPASy, EBI, Israel, Japan]

Frodl R., Gierschik P., Moepps B.;

"Genomic organization and expression of the CXCR4 gene in mouse and man: absence of a splice variant corresponding to mouse CXCR4-B in human tissues.";

J. Recept. Signal Transduct. Res. 18:321-344(1998).

[11] SEQUENCE FROM NUCLEIC ACID (ISOFORM 2).

**SPECIES**=Human;

**TISSUE**=Neutrophils;

MEDLINE=99384048; PubMed=10452968; [NCBI, ExPASy, EBI, Israel, Japan]

Gupta S.K., Pillarisetti K.;

"CXCR4-Lo: molecular cloning and functional expression of a novel human CXCR4 splice variant.";  
J. Immunol. 163:2368-2372(1999).

[12] SEQUENCE FROM NUCLEIC ACID.

**SPECIES**=P.troglodytes;

MEDLINE=98090115; PubMed=9430250; [NCBI, ExPASy, EBI, Israel, Japan]

Pretet J.-L., Zerbib A.C., Girard M., Guillet J.-G., Butor C.;

"Chimpanzee CXCR4 and CCR5 act as coreceptors for HIV type 1.";  
AIDS Res. Hum. Retroviruses 13:1583-1587(1997).

[13] SULFATION.

**SPECIES**=Human;

MEDLINE=99189752; PubMed=10089882; [NCBI, ExPASy, EBI, Israel, Japan]

Farzan M., Mirzabekov T., Kolchinsky P., Wyatt R., Cayabyab M., Gerard N.P., Gerard C., Sodroski J., Choe H.;

"Tyrosine sulfation of the amino terminus of CCR5 facilitates HIV-1 entry.";  
Cell 96:667-676(1999).

[14] FUNCTION.

MEDLINE=96351077; PubMed=8752280; [NCBI, ExPASy, EBI, Israel, Japan]

Bleul C.C., Farzan M., Choe H., Parolin C., Clark-Lewis I., Sodroski J., Springer T.A.;

"The lymphocyte chemoattractant SDF-1 is a ligand for LESTR/fusin and blocks HIV-1 entry.";  
Nature 382:829-833(1996).

[15] FUNCTION.

MEDLINE=96351078; PubMed=8752281; [NCBI, ExPASy, EBI, Israel, Japan]

Oberlin E., Amara A., Bachelier F., Bessia C., Virelizier J.-L., Arenzana-Seisdedos F., Schwartz O., Heard J.-M.,  
Clark-Lewis I., Legler D.F., Loetscher M., Baggiolini M., Moser B.;

"The CXCR4 chemokine SDF-1 is the ligand for LESTR/fusin and prevents infection by T-cell-line-adapted HIV-1.";  
Nature 382:833-835(1996).

[16] ERRATUM.

Oberlin E., Amara A., Bachelier F., Bessia C., Virelizier J.-L., Arenzana-Seisdedos F., Schwartz O., Heard J.-M.,  
Clark-Lewis I., Legler D.F., Loetscher M., Baggiolini M., Moser B.;

Nature 384:288-288(1996).

[17] CHARACTERIZATION OF ITS HIV-1 CORECEPTOR FUNCTION.

MEDLINE=97002453; PubMed=8849450; [NCBI, ExPASy, EBI, Israel, Japan]

Lapham C.K., Ouyang J., Chandrasekhar B., Nguyen N.Y., Dimitrov D.S., Golding H.;

"Evidence for cell-surface association between fusin and the CD4-gp120 complex in human cell lines.";  
Science 274:602-605(1996).

[18] CHARACTERIZATION OF ITS HIV-2 RECEPTOR FUNCTION.

MEDLINE=97083584; PubMed=8929542; [NCBI, ExPASy, EBI, Israel, Japan]

Endres M.J., Clapham P.R., Marsh M., Ahuja M., Turner J.D., McKnight A., Thomas J.F., Stoeckenau-Haggarty B.,  
Choe S., Vance P.J., Wells T.N.C., Power C.A., Sutterwala S.S., Doms R.W., Landau N.R., Hoxie J.A.;

"CD4-independent infection by HIV-2 is mediated by fusin/CXCR4.";  
Cell 87:745-756(1996).

**Comments**

- **FUNCTION:** RECEPTOR FOR THE C-X-C CHEMOKINE SDF-1. TRANSDUCES A SIGNAL BY INCREASING THE INTRACELLULAR CALCIUM IONS LEVEL. INVOLVED IN HAEMATOPOIESIS AND IN CARDIAC VENTRICULAR SEPTUM FORMATION. PLAYS ALSO AN ESSENTIAL ROLE IN VASCULARIZATION OF THE GASTROINTESTINAL TRACT, PROBABLY BY REGULATING VASCULAR BRANCHING AND/OR REMODELLING PROCESSES IN ENDOTHELIAL CELLS. COULD BE INVOLVED IN CEREBELLAR DEVELOPMENT. IN THE CNS, COULD MEDIATE HIPPOCAMPAL-NEURON SURVIVAL. ACTS AS A PRIMARY RECEPTOR FOR SOME HIV-2 ISOLATES AND AS A CO-RECEPTOR WITH CD4 FOR HIV-1 X4 VIRUSES (LYMPHOCYTE-TROPIC HIV-1 VIRUSES, ALSO CALLED SYNCYTIIUM-INDUCING (SI) STRAINS). PROMOTES ENV-MEDIATED FUSION OF THE VIRUS.
- **SUBCELLULAR LOCATION:** Integral membrane protein.
- **ALTERNATIVE PRODUCTS:** At least 2 isoforms; 1 (shown here) and 2/CXCR4-LO; are produced by alternative splicing. Isoform 2 has been shown to exist only in human so far.
- **TISSUE SPECIFICITY:** Expressed in numerous tissues, such as peripheral blood leukocytes, spleen, thymus, spinal cord, heart, placenta, lung, liver, skeletal muscle, kidney, pancreas, cerebellum, cerebral cortex and medulla (in microglia as well as in astrocytes), brain microvascular, coronary artery and umbilical cord endothelial cells. Isoform 1

is predominant in all tissues tested.

- **PTM:** SULFATED.
- **SIMILARITY:** BELONGS TO FAMILY 1 OF G-PROTEIN COUPLED RECEPTORS.
- **CAUTION:** WAS ORIGINALLY (REF.1 AND REF.2) THOUGHT TO BE A RECEPTOR FOR NEUROPEPTIDE Y, TYPE 3 (NPY3-R).
- **DATABASE:** NAME=PROW; NOTE=PROW 2:50-58(2001);  
WWW="[http://www.ncbi.nlm.nih.gov/prow/guide/192999234\\_g.htm](http://www.ncbi.nlm.nih.gov/prow/guide/192999234_g.htm)".

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### Cross-references

EMBL	L01639; AAA16594.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	M99293; AAA16617.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	X71635; CAA50641.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	L06797; AAA03209.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	D10924; BAA01722.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF005058; AAB93982.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF052572; AAC34581.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF025375; AAB81970.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	Y14739; CAA75034.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AJ224869; CAA12166.1; ALT_SEQ. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF147204; AAF00130.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	U89798; AAC03718.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	S32761; S32761.
A45747; A45747.	
Genew	HGNC:2561; CXCR4.
CleanEx	HGNC:2561; CXCR4.
MIM	162643 [NCBI / EBI].
GeneCards	CXCR4.
GeneLynx	CXCR4; Homo sapiens.
SOURCE	CXCR4; Homo sapiens.
Ensembl	P30991; Homo sapiens. [Entry / Contig view]
InterPro	IPR000276; GPCR_Rhodpsn.
	Graphical view of domain structure.
Pfam	PF00001; 7tm_1; 1.
PRINTS	PR00237; GPCRRHODOPSN.
PROSITE	PS00237; G_PROTEIN_RECEP_F1_1; 1.
	PS50262; G_PROTEIN_RECEP_F1_2; 1.
GPCRDB	P30991; CCR4_HUMAN.
GPCRDB-Snakes	P30991.
ProDom	[Domain structure / List of seq. sharing at least 1 domain].
BLOCKS	P30991.
ProtoNet	P30991.
ProtoMap	P30991.
PRESAGE	P30991.
DIP	P30991.
ModBase	P30991.
SWISS-2DPAGE	Get region on 2D PAGE.

### Keywords

**G-protein coupled receptor; Transmembrane; Glycoprotein; Sulfation; Antigen; Alternative splicing.**

### Features

Key	From	To	Length	Description
DOMAIN	1	39	39	EXTRACELLULAR (POTENTIAL).
TRANSMEM	40	63	24	1 (POTENTIAL).
DOMAIN	64	79	16	CYTOPLASMIC (POTENTIAL).
TRANSMEM	80	99	20	2 (POTENTIAL).
DOMAIN	100	110	11	EXTRACELLULAR (POTENTIAL).
TRANSMEM	111	132	22	3 (POTENTIAL).
DOMAIN	133	154	22	CYTOPLASMIC (POTENTIAL).
TRANSMEM	155	175	21	4 (POTENTIAL).
DOMAIN	176	200	25	EXTRACELLULAR (POTENTIAL).
TRANSMEM	201	220	20	5 (POTENTIAL).
DOMAIN	221	240	20	CYTOPLASMIC (POTENTIAL).
TRANSMEM	241	261	21	6 (POTENTIAL).
DOMAIN	262	285	24	EXTRACELLULAR (POTENTIAL).
TRANSMEM	286	305	20	7 (POTENTIAL).
DOMAIN	306	352	47	CYTOPLASMIC (POTENTIAL).
MOD_RES	21	21		SULFATION (POTENTIAL).
CARBOHYD	11	11		N-LINKED (GLCNAC...) (POTENTIAL).
DISULFID	109	186		BY SIMILARITY.
VARSP LIC	1	5		MEGIS -> MSIPLPLLQ (IN ISOFORM 2).


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### Sequence information

Length: 352 AA Molecular weight: 39745 Da CRC64: 8C8476A186786B83 [This is a checksum on the sequence]

```

      10      20      30      40      50      60
      |      |      |      |      |      |
MEGISIYTSN NYTEEMSGD YDSMKEPCFR EENANFNKIF LPTIYSIIFL TGIVGNGLVI
      70      80      90     100     110     120
      |      |      |      |      |      |
LVMGYQKKLR SMTDKYRLHL SVADLLFVIT LPFWAVDAVA NWYFGNFLCK AVHVIYTVNL
     130     140     150     160     170     180
      |      |      |      |      |      |
YSSVLILAFI SLDRYLAIVH ATNSQRPRKL LAEKVVYVGV WIPALLLTIP DFIFANVSEA
     190     200     210     220     230     240
      |      |      |      |      |      |
DDRYICDRFY PNDLVVVVFQ FQHIMVGLIL PGIVILSCYC IIISKLSHSK GHQKRKALKT
     250     260     270     280     290     300
      |      |      |      |      |      |
TVILILAFFA CWLPYYIGIS IDSFILLEII KQGCEFENTV HKWISITEAL AFFHCCLNPI
     310     320     330     340     350
      |      |      |      |      |
LYAFLGAKFK TSAQHALTSV SRGSSLKILS KGKRGHSSV STESESSSFH SS

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